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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,828	06/26/2006	Tsutomu Ishihara	KPO-LTT-P5/LTT-98/US	1014

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EXAMINER	
DICKINSON, PAUL W	

ART UNIT	PAPER NUMBER
1618	

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04/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,828	ISHIHARA ET AL.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *20-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/16/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (Claim 1-19) in the reply filed on 2/25/2008 is acknowledged.

Claims 1-19 are currently under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-5 and 11-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3 and 4 recite the phrase "negative ion residue". These claims and the claims that depend from them do not meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information. The specification provides insufficient written description to support the genus of negative ion residues encompassed by the claim, since there is no description of the structural relationship of these residues provided in the specification and Applicant has not provided a

description as to how the base molecule may be changed while remaining a residue. The chemical structures encompassed by this genus are highly variant and encompass a myriad of possibilities.

The appearance of mere indistinct words (here the word "inhibitor") in a specification or a claim, even an original claim, does not necessarily satisfy the written description requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004). A description of what a material does, rather than of what it is, usually does not suffice to provide an adequate written description of the invention. Univ. of Cal. v. Eli Lilly, 119 F.3d 1559, 1568 (Fed. Cir. 1997). Furthermore, to the extent that a functional description can meet the requirement for an adequate written description, it can do so only in accordance with PTO guidelines stating that the requirement can be met by disclosing "sufficiently detailed, relevant identifying characteristics," including "functional characteristics when coupled with a known or disclosed correlation between function and structure." Univ. of Rochester v. G.D. Searle, 68 USPQ2d 1424, 1432 (DC WNY 2003). No such correlation has been disclosed here; at best all that can be inferred from the instant specification is that compounds having the general formulae set forth at page 5 of the specification inhibit the production of downstream products of 14 kD PLA2, such as arachidonic acid. See the first paragraph on page 13. Whether this was specifically due to inhibition of enzyme activity, or also due inhibition of production, transcription or translation, or some combination of these, is not clear from the data presented.

The examiner recognizes that the fact situation in the Rochester cases was extreme, with Applicant disclosing there no (or possibly one) specific compounds. The reasoning provided by the court can be fairly extended to less extreme situations (*i.e.*, where a limited number of species is actually disclosed, such as here), however, given the court's recognition that:

> [I]n claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. Rochester (2003) at 1431.

As was the case in Rochester, there is no such specificity here, nor could one skilled in the art identify any particular compound, other than those having the general formula set forth at the top of page 5 of the specification, as being able to inhibit any particular mechanism of 14 kDa PLA_2 action, other than to inhibit its "activity" in some unspecified way.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 6, 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9941298 (hereafter WO '298; US 6685966 ('966) is an English equivalent and will be referenced hereafter). WO '298 discloses drug-containing nanoparticles

provided by causing primary nanoparticles containing a hydrophobic active material (fat-soluble drug) to act with alkaline earth metal salts (bivalent metal salts) to give secondary nanoparticles, and causing bases such as sodium hydroxide or potassium hydroxide (a monovalent basic salt) to act with the secondary particles (see '966: col 1, lines 51-61; col 4, lines 39-65; col 7, lines 34-35; Examples 1-2). The exemplified nanoparticles are prepared by causing the primary particles to act with calcium chloride to give secondary nanoparticles and causing sodium hydroxide to act with the secondary nanoparticles (see '996: Example 2).

Claims 1, 3 and 11-18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 03033592 (hereafter WO '592). WO '592 discloses drug-containing polymeric micelles (nanoparticles) wherein primary nanoparticles are produced by causing a hydrophobic drug (a fat-soluble drug where paclitaxel (MW=854 daltons) and cyclosporine are exemplified) to act with carboxyl terminated polylactic acid (a long chain organic compound having a negative ion residue) and a block copolymer of polyethylene glycol and polylactic acid (a surfactant), and the primary nanoparticles are subsequently allowed to act with di- or tri-valent metal salts (Ca^{2+} salts are exemplified) (see abstract; page 3, lines 16-30; Figures 3-5; Examples 1-13).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 03033592 (hereafter WO '592) in view of US 3701745 (hereafter '745). As stated above, WO '592 discloses drug-containing polymeric micelles (nanoparticles) wherein

primary nanoparticles are produced by causing a hydrophobic drug (a fat-soluble drug) to act with carboxyl terminated polylactic acid (a long chain organic compound having a negative ion residue) and a block copolymer of polyethylene glycol and polylactic acid (a surfactant), and the primary nanoparticles are subsequently allowed to act with di- or tri-valent metal salts (Ca^{2+} salts are exemplified). WO '592 fails to disclose incorporation of a C_8-C_{24} fatty acid or its salt.

'745 teaches that oleic acid, a long chain organic compound having a negative ion residue, is a useful component in polymeric micelle compositions (see col 3, line 59).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the carboxyl terminated polylactic acid in the nanoparticles disclosed by WO '592 with oleic acid, because both compounds are structural and functional equivalents, with a reasonable expectation of success, to afford improved drug-containing polymeric micelles.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9941298 (hereafter WO '298; US 6685966 ('966) is an English equivalent and will be referenced hereafter) in view of US 6159381 (hereafter '381). As stated above, WO '298 discloses drug-containing nanoparticles provided by causing primary nanoparticles containing a hydrophobic active material (fat-soluble drug) to act with alkaline earth metal salts (bivalent metal salts) to give secondary nanoparticles, and causing bases such as sodium hydroxide (a monovalent basic salt) to act with the secondary particles.

'966 discloses that the purpose of adding the base is to cause the alkaline earth metal salt to precipitate (see '996: col 4, lines 52-54). The disclosed nanoparticles are a useful encapsulation system appropriate for the packaging of a hydrophobic active material and for its release in a controlled way (see '996: col 1, lines 1-11). WO '298 fails to disclose a base selected from hydrogen carbonates, hydrogen phosphates, carbonates, phosphates, oxalates, lactates, and urates.

'381 teaches that carbonates are used in the art to cause alkaline earth metal salts to precipitate from aqueous solutions (see abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute a carbonate salt, a base which causes alkaline earth metal salts to precipitate from aqueous solutions, for the sodium hydroxide, a base which causes alkaline earth metal salts to precipitate from aqueous solutions, in the nanoparticles disclosed by WO '298, with a reasonable expectation of success, to afford an improved encapsulation system appropriate for the packaging of a hydrophobic active material and for its release in a controlled way.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9941298 (hereafter WO '298; US 6685966 ('966) is an English equivalent and will be referenced hereafter). As stated above, WO '298 discloses drug-containing nanoparticles provided by causing primary nanoparticles containing a hydrophobic active material (fat-soluble drug) to act with alkaline earth metal salts (bivalent metal salts) to give secondary nanoparticles, and causing bases such as sodium hydroxide or

potassium hydroxide (a monovalent basic salt) to act with the secondary particles. The exemplified nanoparticles are prepared by causing the primary particles to act with calcium chloride to give secondary nanoparticles and causing sodium hydroxide to act with the secondary nanoparticles. WO '298 discloses particle diameters of 0.03 to 10 microns (30 to 10,000 nanometers) and the exempflied nanoparticles have a particle diameter of about 0.21 microns (210 nanometers) (see '996: col 3, line 11; Examples 1-2). WO '298 fails to disclose a particle diameter range of 1 to 200 nanometers.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the particle diameter with a reasonable expectation of success to afford nanoparticles with the instantly disclosed particle diameter range that are an improved encapsulation system appropriate for the packaging of a hydrophobic active material and for its release in a controlled way.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

March 28, 2008